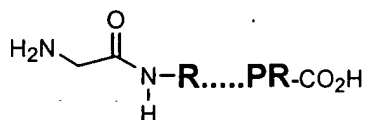
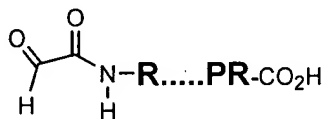
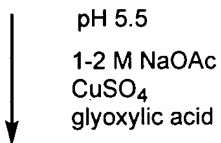


09/590,592



Domain 1 of  $\beta_2\text{GPI}$  ( $\text{D}_1$ , where bold letters stand for single letter amino acid code of terminal amino acids of Domain 1 of  $\beta_2\text{GPI}$ )



Transaminated Domain 1 (**TA/D1**)  
 Comprising a terminal glyoxyl group

Figure 1

008090-26506560

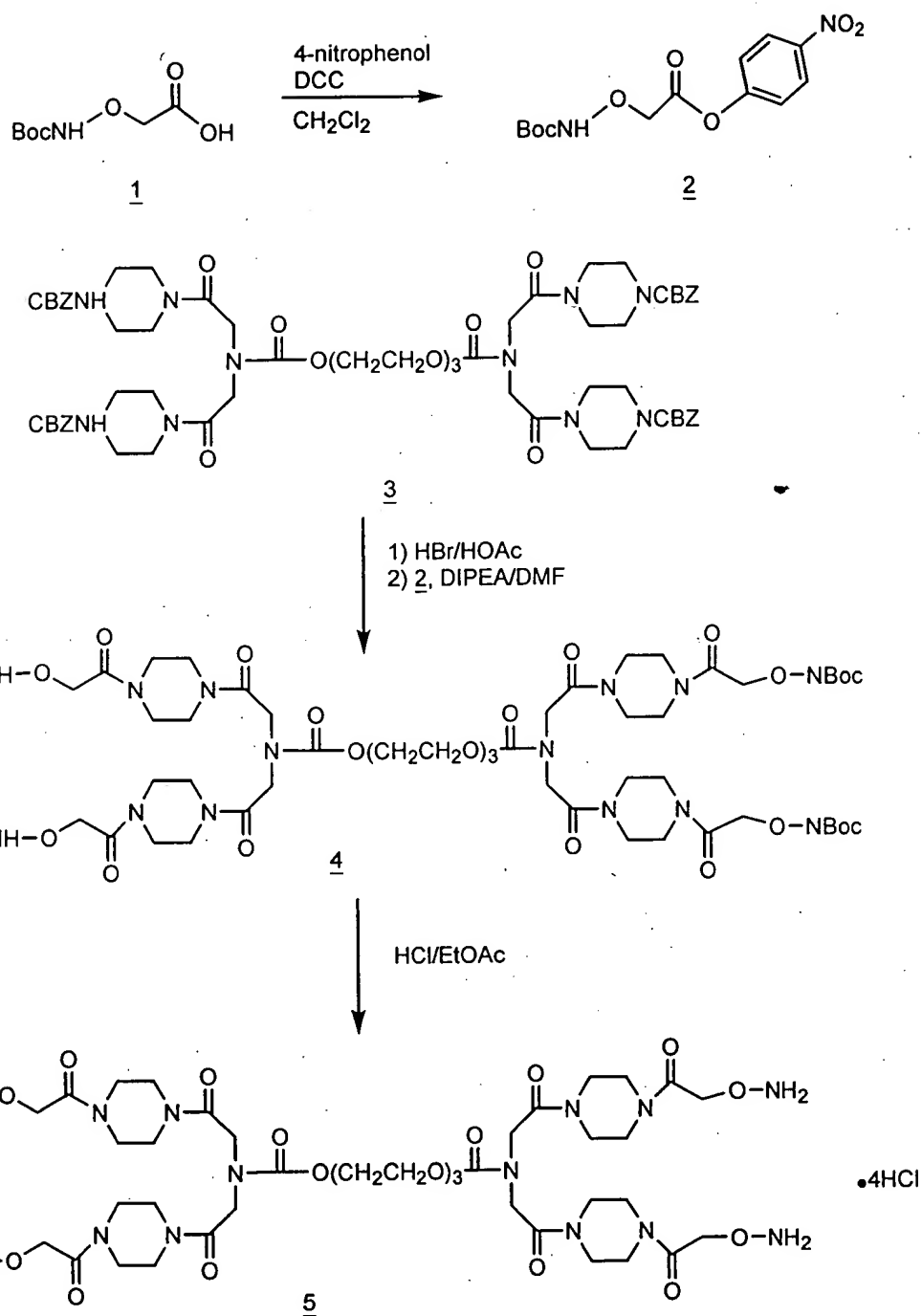


Figure 2

003030" 26506560

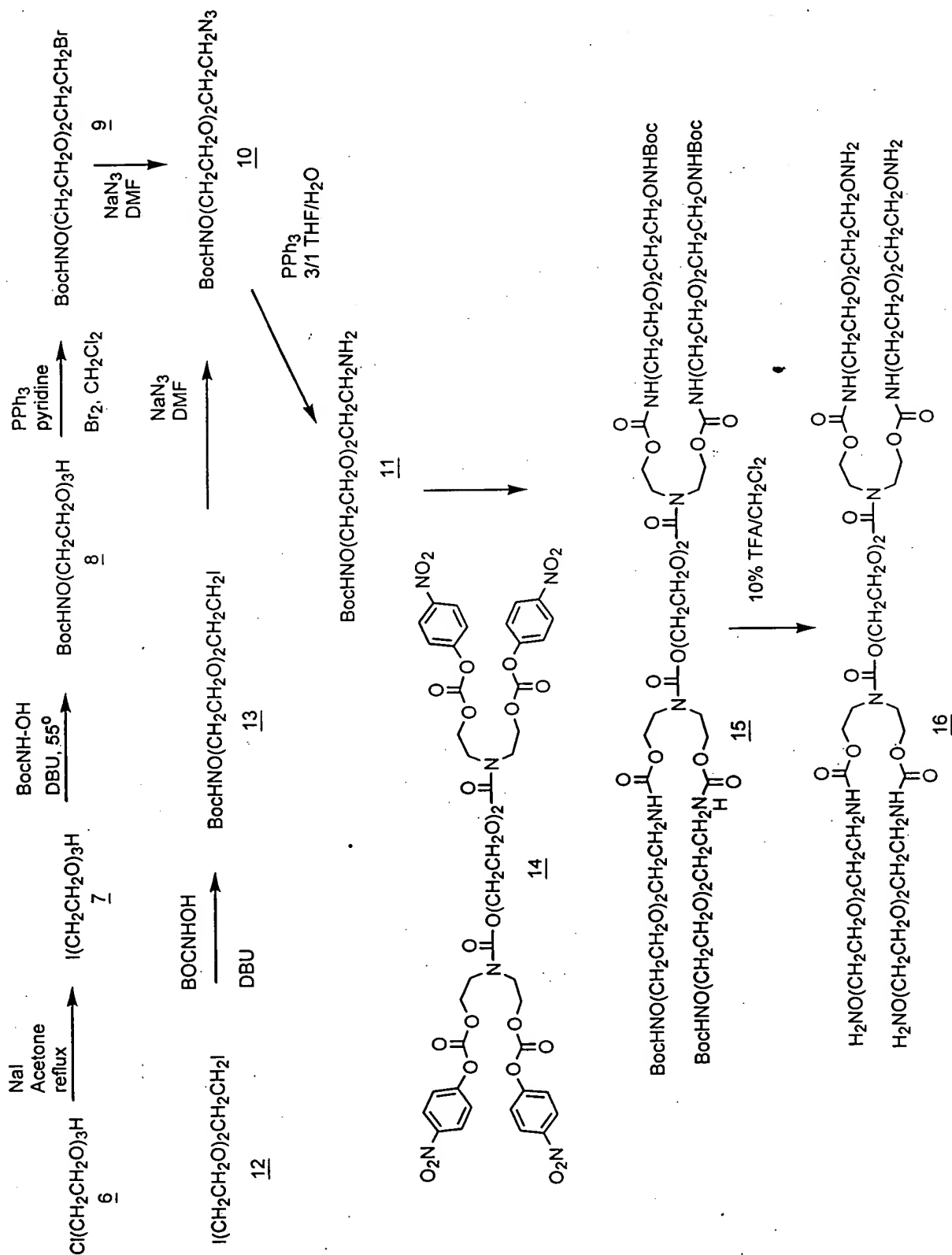


Figure 3

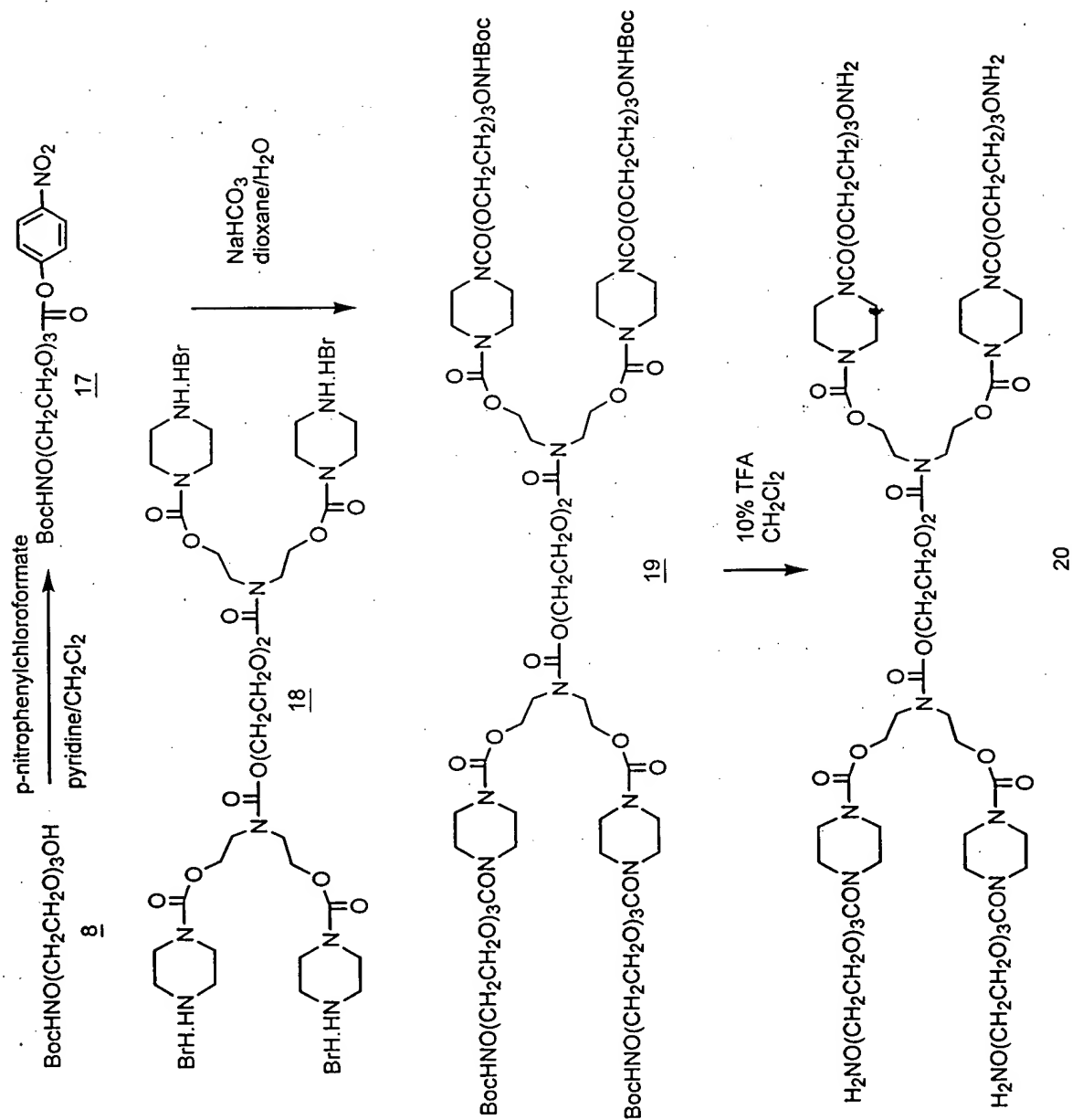


Figure 4

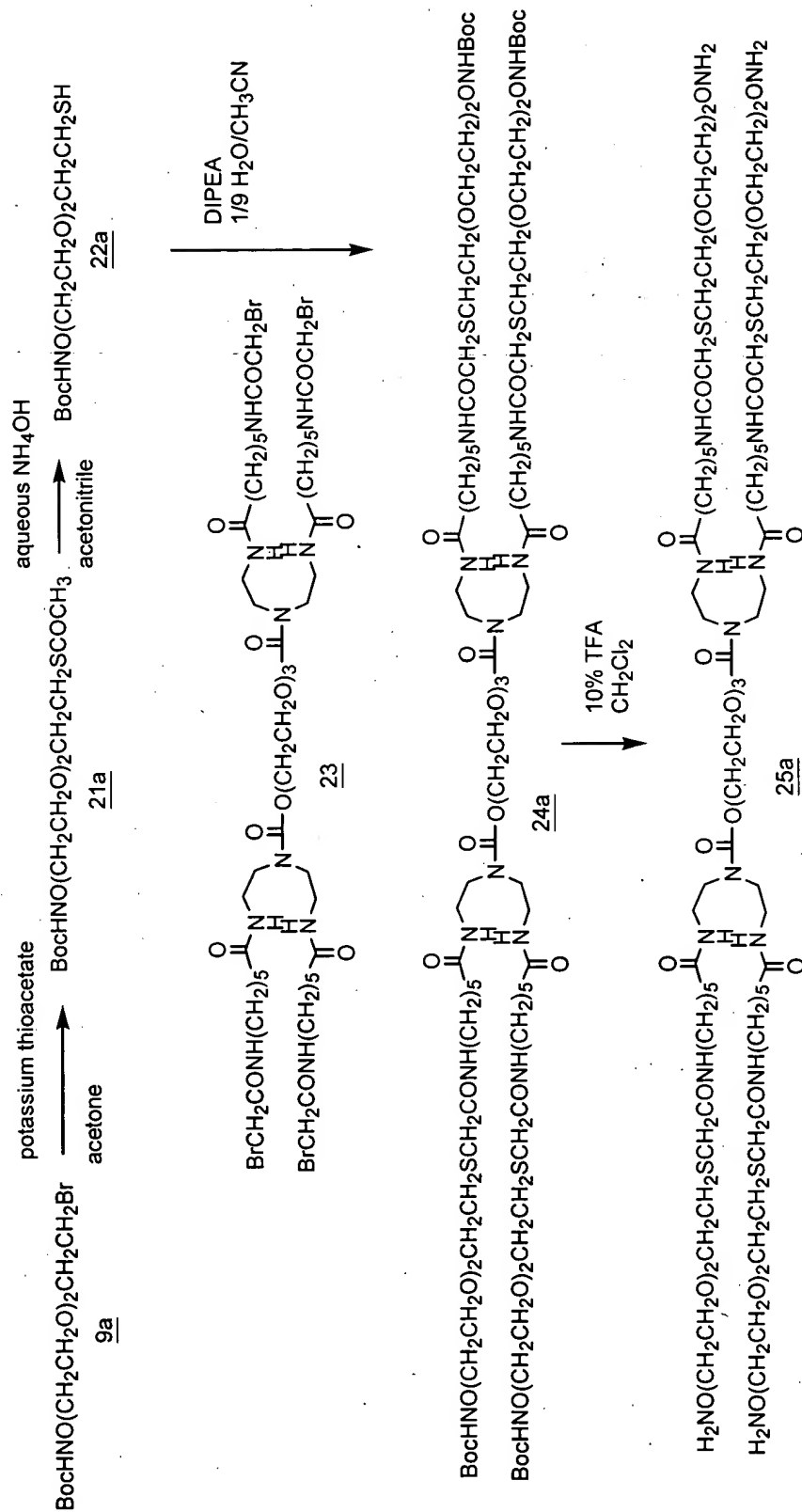


Figure 5

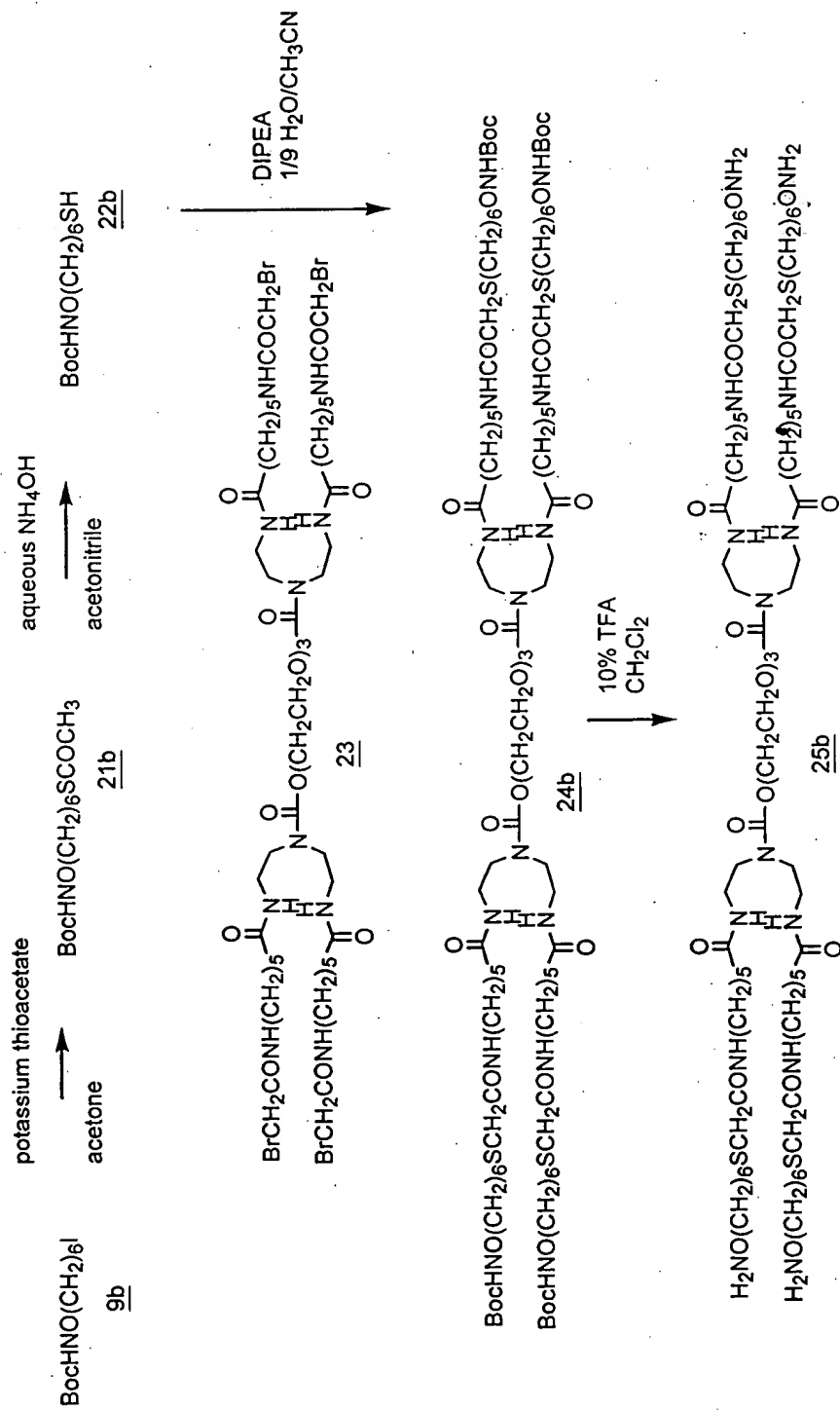


Figure 6

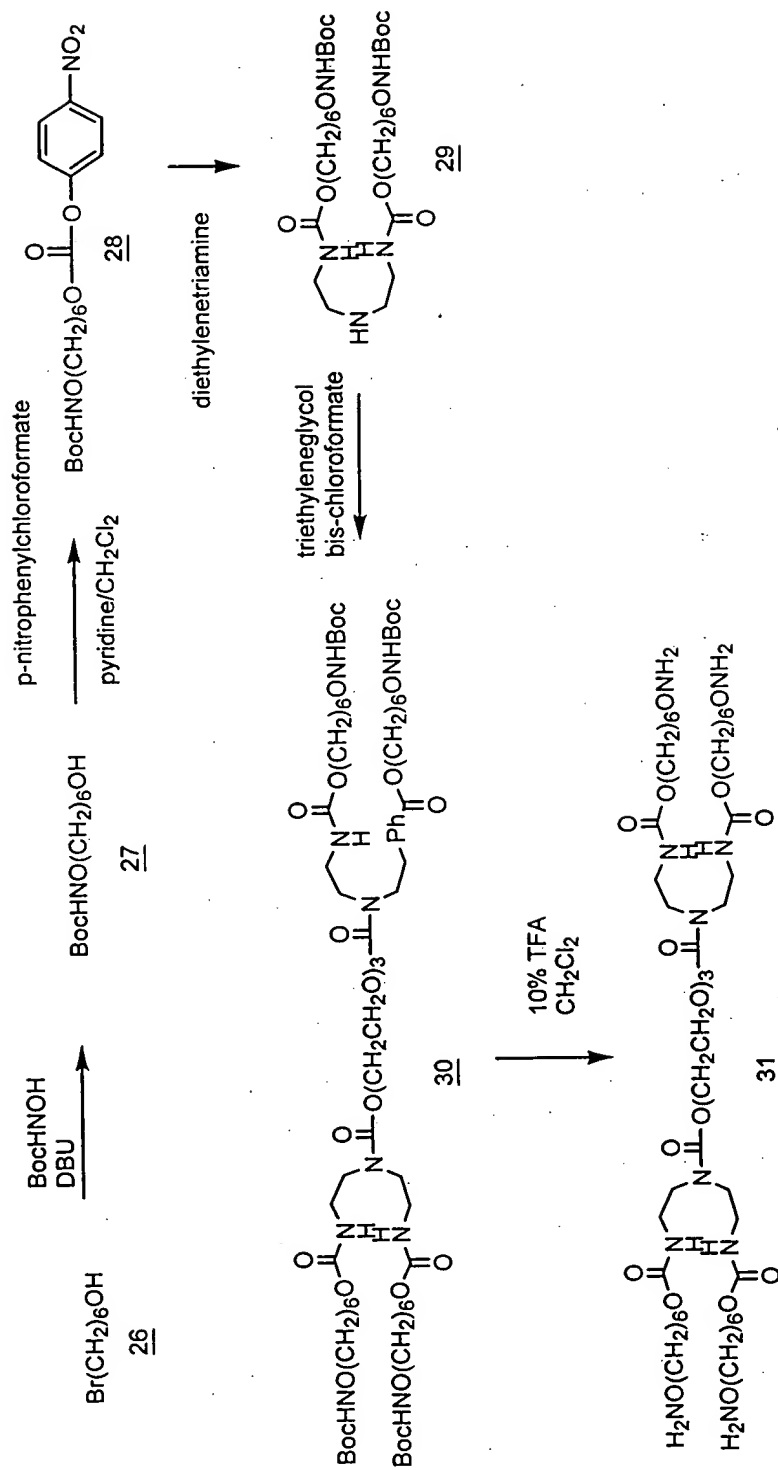


Figure 7

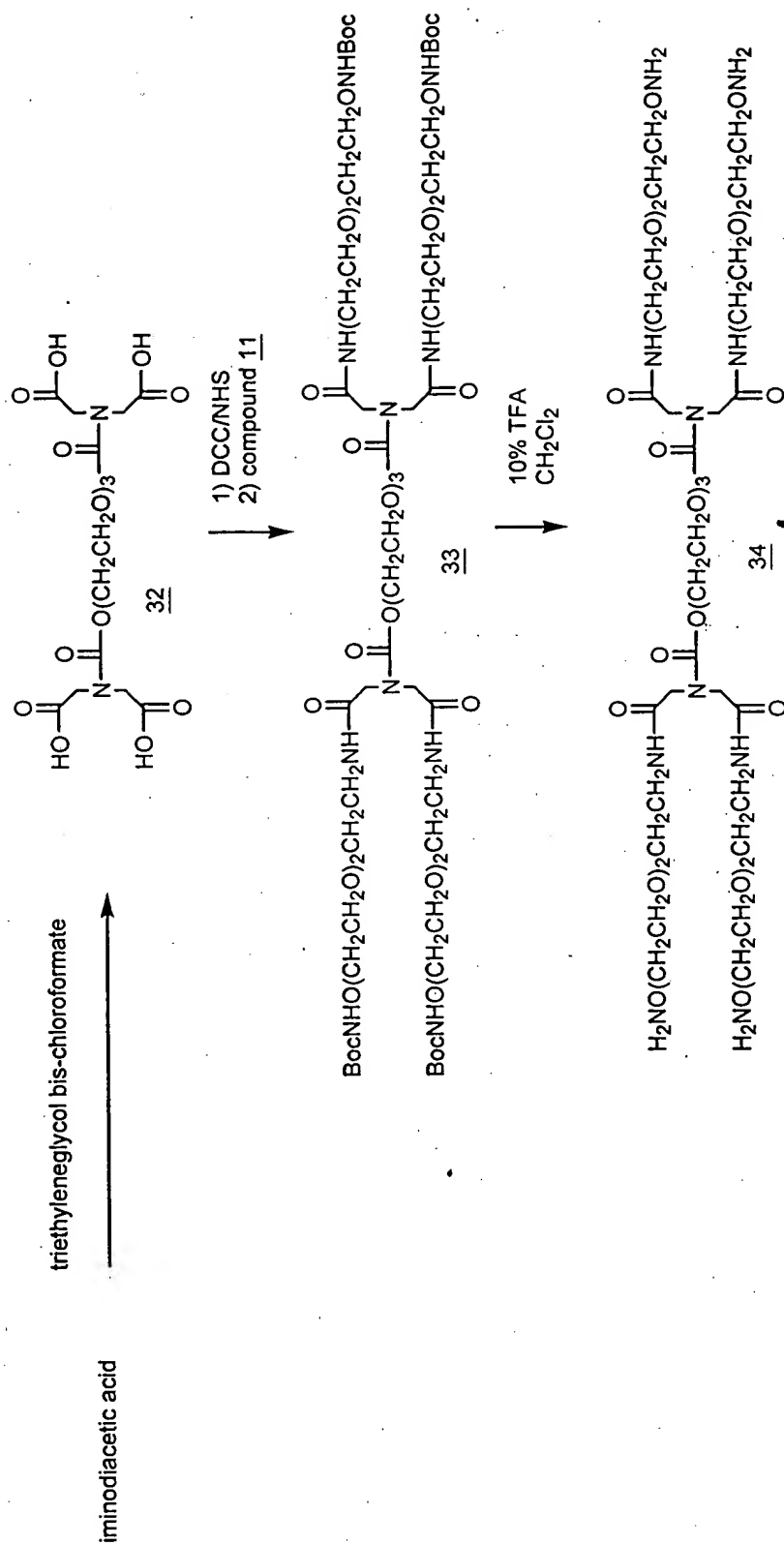


Figure 8



CC(=O)CCC(=O)O
 $\xrightarrow{\text{4-nitrophenyltrifluoroacetate, pyridine}}$ 
CC(=O)CCC(=O)Oc1ccc([N+](=O)[O-])cc1
  
35

12
 $\xrightarrow{\text{BocNHOH/DBU}}$ 
BocNHO(CH2CH2O)2CH2CH2ONHBoc
 $\xrightarrow{\text{HCl, EtOAc}}$ 
H2NO(CH2CH2O)2CH2CH2ONH2
  
36
37

3
 $\xrightarrow{\begin{array}{l} 1) \text{ HBr/HOAc} \\ 2) \text{ 35, NaHCO}_3/\text{H}_2\text{O} \end{array}}$

CC(=O)CCC(=O)N1CCN(CC1)C(=O)N(C(=O)N2CCN(CC2)C(=O)N(C(=O)N3CCN(CC3)C(=O)N(C(=O)N4CCN(CC4)C(=O)N(C(=O)N5CCN(CC5)C(=O)N(C(=O)N6CCN(CC6)C(=O)N(C(=O)N7CCN(CC7)C(=O)N(C(=O)N8CCN(CC8)C(=O)N(C(=O)N9CCN(CC9)C(=O)N(C(=O)N10CCN(CC10)C(=O)N(C(=O)N11CCN(CC11)C(=O)N(C(=O)N12CCN(CC12)C(=O)N(C(=O)N13CCN(CC13)C(=O)N(C(=O)N14CCN(CC14)C(=O)N(C(=O)N15CCN(CC15)C(=O)N(C(=O)N16CCN(CC16)C(=O)N(C(=O)N17CCN(CC17)C(=O)N(C(=O)N18CCN(CC18)C(=O)N(C(=O)N19CCN(CC19)C(=O)N(C(=O)N20CCN(CC20)C(=O)N(C(=O)N21CCN(CC21)C(=O)N(C(=O)N22CCN(CC22)C(=O)N(C(=O)N23CCN(CC23)C(=O)N(C(=O)N24CCN(CC24)C(=O)N(C(=O)N25CCN(CC25)C(=O)N(C(=O)N26CCN(CC26)C(=O)N(C(=O)N27CCN(CC27)C(=O)N(C(=O)N28CCN(CC28)C(=O)N(C(=O)N29CCN(CC29)C(=O)N(C(=O)N30CCN(CC30)C(=O)N(C(=O)N31CCN(CC31)C(=O)N(C(=O)N32CCN(CC32)C(=O)N(C(=O)N33CCN(CC33)C(=O)N(C(=O)N34CCN(CC34)C(=O)N(C(=O)N35CCN(CC35)C(=O)N(C(=O)N36CCN(CC36)C(=O)N(C(=O)N37CCN(CC37)C(=O)N(C(=O)N38CCN(CC38)C(=O)N(C(=O)N39CCN(CC39)C(=O)N(C(=O)N40CCN(CC40)C(=O)N(C(=O)N41CCN(CC41)C(=O)N(C(=O)N42CCN(CC42)C(=O)N(C(=O)N43CCN(CC43)C(=O)N(C(=O)N44CCN(CC44)C(=O)N(C(=O)N45CCN(CC45)C(=O)N(C(=O)N46CCN(CC46)C(=O)N(C(=O)N47CCN(CC47)C(=O)N(C(=O)N48CCN(CC48)C(=O)N(C(=O)N49CCN(CC49)C(=O)N(C(=O)N50CCN(CC50)C(=O)N(C(=O)N51CCN(CC51)C(=O)N(C(=O)N52CCN(CC52)C(=O)N(C(=O)N53CCN(CC53)C(=O)N(C(=O)N54CCN(CC54)C(=O)N(C(=O)N55CCN(CC55)C(=O)N(C(=O)N56CCN(CC56)C(=O)N(C(=O)N57CCN(CC57)C(=O)N(C(=O)N58CCN(CC58)C(=O)N(C(=O)N59CCN(CC59)C(=O)N(C(=O)N60CCN(CC60)C(=O)N(C(=O)N61CCN(CC61)C(=O)N(C(=O)N62CCN(CC62)C(=O)N(C(=O)N63CCN(CC63)C(=O)N(C(=O)N64CCN(CC64)C(=O)N(C(=O)N65CCN(CC65)C(=O)N(C(=O)N66CCN(CC66)C(=O)N(C(=O)N67CCN(CC67)C(=O)N(C(=O)N68CCN(CC68)C(=O)N(C(=O)N69CCN(CC69)C(=O)N(C(=O)N70CCN(CC70)C(=O)N(C(=O)N71CCN(CC71)C(=O)N(C(=O)N72CCN(CC72)C(=O)N(C(=O)N73CCN(CC73)C(=O)N(C(=O)N74CCN(CC74)C(=O)N(C(=O)N75CCN(CC75)C(=O)N(C(=O)N76CCN(CC76)C(=O)N(C(=O)N77CCN(CC77)C(=O)N(C(=O)N78CCN(CC78)C(=O)N(C(=O)N79CCN(CC79)C(=O)N(C(=O)N80CCN(CC80)C(=O)N(C(=O)N81CCN(CC81)C(=O)N(C(=O)N82CCN(CC82)C(=O)N(C(=O)N83CCN(CC83)C(=O)N(C(=O)N84CCN(CC84)C(=O)N(C(=O)N85CCN(CC85)C(=O)N(C(=O)N86CCN(CC86)C(=O)N(C(=O)N87CCN(CC87)C(=O)N(C(=O)N88CCN(CC88)C(=O)N(C(=O)N89CCN(CC89)C(=O)N(C(=O)N90CCN(CC90)C(=O)N(C(=O)N91CCN(CC91)C(=O)N(C(=O)N92CCN(CC92)C(=O)N(C(=O)N93CCN(CC93)C(=O)N(C(=O)N94CCN(CC94)C(=O)N(C(=O)N95CCN(CC95)C(=O)N(C(=O)N96CCN(CC96)C(=O)N(C(=O)N97CCN(CC97)C(=O)N(C(=O)N98CCN(CC98)C(=O)N(C(=O)N99CCN(CC99)C(=O)N(C(=O)N100CCN(CC100)C(=O)N(C(=O)N101CCN(CC101)C(=O)N(C(=O)N102CCN(CC102)C(=O)N(C(=O)N103CCN(CC103)C(=O)N(C(=O)N104CCN(CC104)C(=O)N(C(=O)N105CCN(CC105)C(=O)N(C(=O)N106CCN(CC106)C(=O)N(C(=O)N107CCN(CC107)C(=O)N(C(=O)N108CCN(CC108)C(=O)N(C(=O)N109CCN(CC109)C(=O)N(C(=O)N110CCN(CC110)C(=O)N(C(=O)N111CCN(CC111)C(=O)N(C(=O)N112CCN(CC112)C(=O)N(C(=O)N113CCN(CC113)C(=O)N(C(=O)N114CCN(CC114)C(=O)N(C(=O)N115CCN(CC115)C(=O)N(C(=O)N116CCN(CC116)C(=O)N(C(=O)N117CCN(CC117)C(=O)N(C(=O)N118CCN(CC118)C(=O)N(C(=O)N119CCN(CC119)C(=O)N(C(=O)N120CCN(CC120)C(=O)N(C(=O)N121CCN(CC121)C(=O)N(C(=O)N122CCN(CC122)C(=O)N(C(=O)N123CCN(CC123)C(=O)N(C(=O)N124CCN(CC124)C(=O)N(C(=O)N125CCN(CC125)C(=O)N(C(=O)N126CCN(CC126)C(=O)N(C(=O)N127CCN(CC127)C(=O)N(C(=O)N128CCN(CC128)C(=O)N(C(=O)N129CCN(CC129)C(=O)N(C(=O)N130CCN(CC130)C(=O)N(C(=O)N131CCN(CC131)C(=O)N(C(=O)N132CCN(CC132)C(=O)N(C(=O)N133CCN(CC133)C(=O)N(C(=O)N134CCN(CC134)C(=O)N(C(=O)N135CCN(CC135)C(=O)N(C(=O)N136CCN(CC136)C(=O)N(C(=O)N137CCN(CC137)C(=O)N(C(=O)N138CCN(CC138)C(=O)N(C(=O)N139CCN(CC139)C(=O)N(C(=O)N140CCN(CC140)C(=O)N(C(=O)N141CCN(CC141)C(=O)N(C(=O)N142CCN(CC142)C(=O)N(C(=O)N143CCN(CC143)C(=O)N(C(=O)N144CCN(CC144)C(=O)N(C(=O)N145CCN(CC145)C(=O)N(C(=O)N146CCN(CC146)C(=O)N(C(=O)N147CCN(CC147)C(=O)N(C(=O)N148CCN(CC148)C(=O)N(C(=O)N149CCN(CC149)C(=O)N(C(=O)N150CCN(CC150)C(=O)N(C(=O)N151CCN(CC151)C(=O)N(C(=O)N152CCN(CC152)C(=O)N(C(=O)N153CCN(CC153)C(=O)N(C(=O)N154CCN(CC154)C(=O)N(C(=O)N155CCN(CC155)C(=O)N(C(=O)N156CCN(CC156)C(=O)N(C(=O)N157CCN(CC157)C(=O)N(C(=O)N158CCN(CC158)C(=O)N(C(=O)N159CCN(CC159)C(=O)N(C(=O)N160CCN(CC160)C(=O)N(C(=O)N161CCN(CC161)C(=O)N(C(=O)N162CCN(CC162)C(=O)N(C(=O)N163CCN(CC163)C(=O)N(C(=O)N164CCN(CC164)C(=O)N(C(=O)N165CCN(CC165)C(=O)N(C(=O)N166CCN(CC166)C(=O)N(C(=O)N167CCN(CC167)C(=O)N(C(=O)N168CCN(CC168)C(=O)N(C(=O)N169CCN(CC169)C(=O)N(C(=O)N170CCN(CC170)C(=O)N(C(=O)N171CCN(CC171)C(=O)N(C(=O)N172CCN(CC172)C(=O)N(C(=O)N173CCN(CC173)C(=O)N(C(=O)N174CCN(CC174)C(=O)N(C(=O)N175CCN(CC175)C(=O)N(C(=O)N176CCN(CC176)C(=O)N(C(=O)N177CCN(CC177)C(=O)N(C(=O)N178CCN(CC178)C(=O)N(C(=O)N179CCN(CC179)C(=O)N(C(=O)N180CCN(CC180)C(=O)N(C(=O)N181CCN(CC181)C(=O)N(C(=O)N182CCN(CC182)C(=O)N(C(=O)

39

$$\begin{array}{c}
 \text{HOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{OH} \\
 | \quad \quad \quad | \\
 \text{N} \quad \quad \quad \text{N} \\
 | \quad \quad \quad | \\
 \text{HOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{OH}
 \end{array}
 \xrightarrow[\text{Br}_2/\text{CH}_2\text{Cl}_2]{\text{PPh}_3/\text{pyridine}}
 \begin{array}{c}
 \text{BrCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{Br} \\
 | \quad \quad \quad | \\
 \text{N} \quad \quad \quad \text{N} \\
 | \quad \quad \quad | \\
 \text{BrCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{Br}
 \end{array}
 \xrightarrow[\text{DBU}]{\text{BocHNOH}}
 \begin{array}{c}
 \text{BocHNOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{ONHBoc} \\
 | \quad \quad \quad | \\
 \text{N} \quad \quad \quad \text{N} \\
 | \quad \quad \quad | \\
 \text{BocHNOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{ONHBoc}
 \end{array}
 \xrightarrow[\text{CH}_2\text{Cl}_2]{10\% \text{ TFA}}
 \begin{array}{c}
 \text{H}_2\text{NOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{ONH}_2 \\
 | \quad \quad \quad | \\
 \text{N} \quad \quad \quad \text{N} \\
 | \quad \quad \quad | \\
 \text{H}_2\text{NOCH}_2\text{CH}_2\text{O} \quad \text{OCH}_2\text{CH}_2\text{ONH}_2
 \end{array}$$

43

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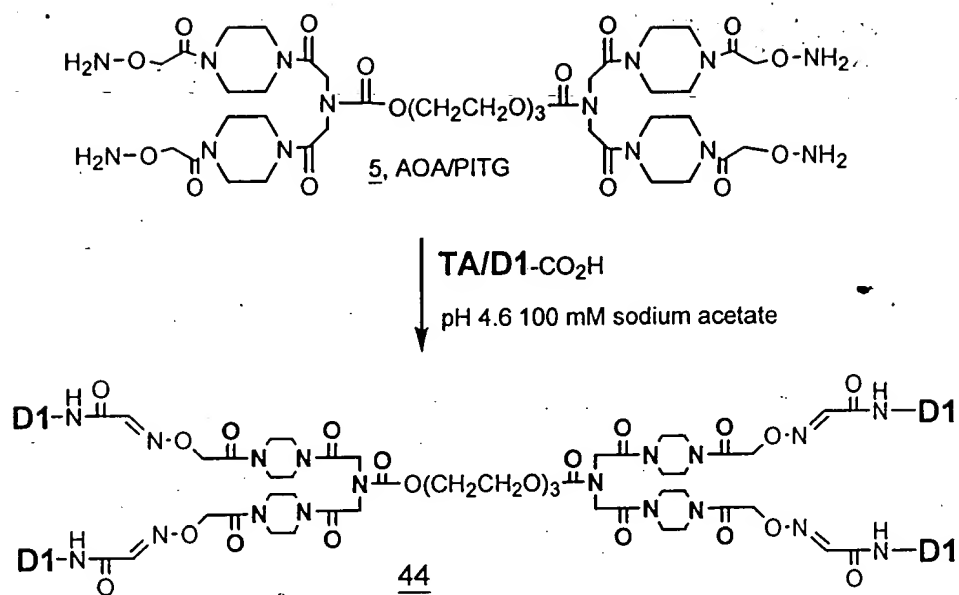


Figure 11



# Comparison of the Rate of Formation of a Peptide Conjugate for AO-TEG-OH & AOA-ADEG-OH

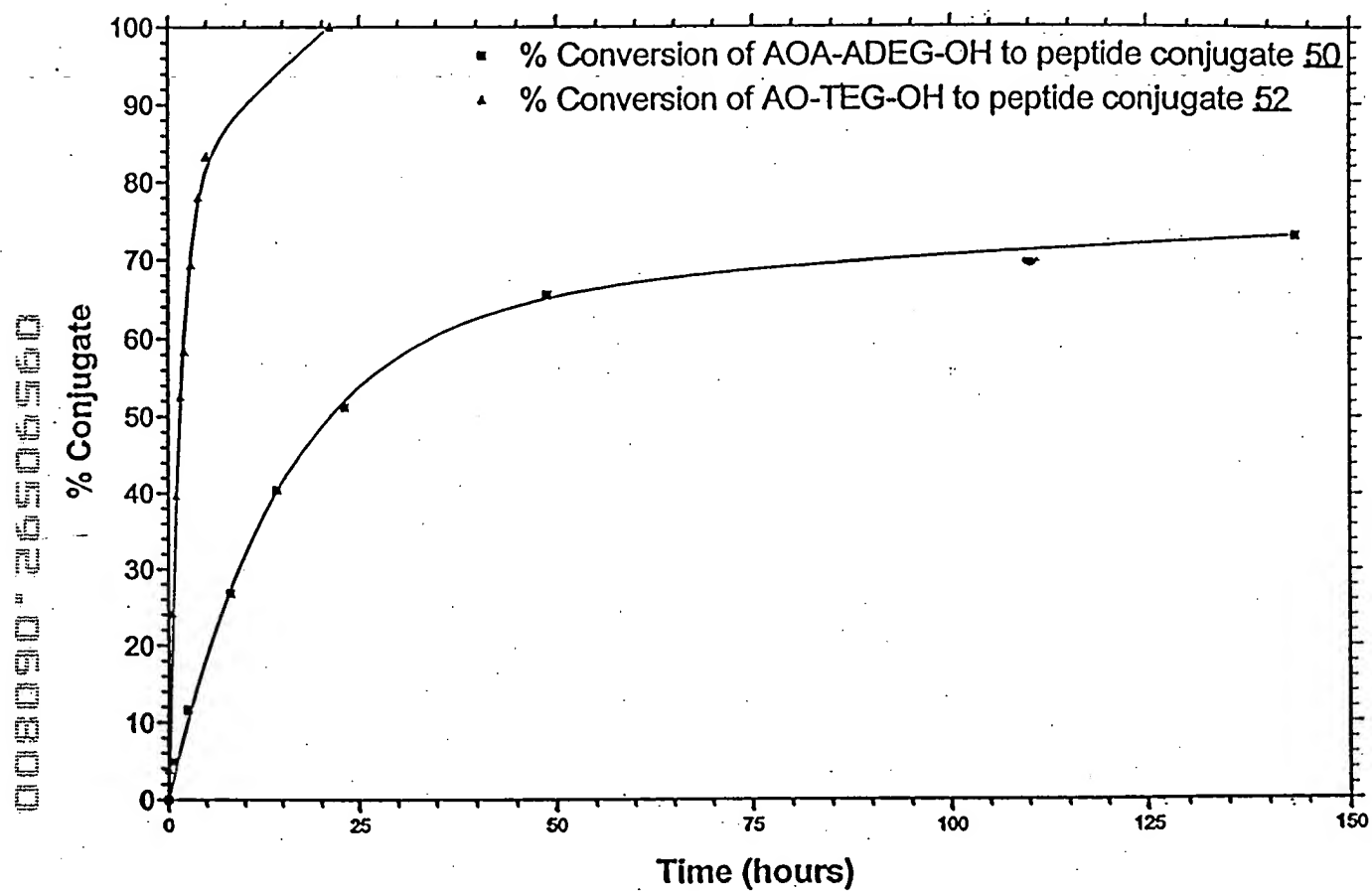
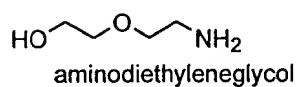
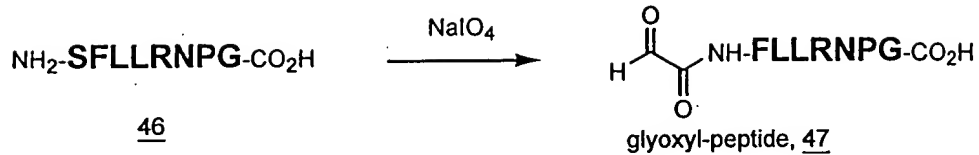
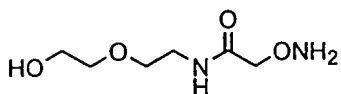


Figure 13

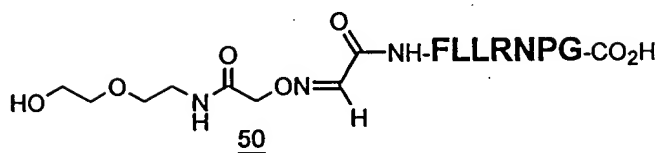


1) compound 2  
 2) TFA



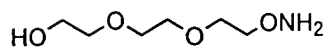
AOA-ADEG-OH, 49

0.1M NaOAC, pH 4.6  
 glyoxyl peptide



Compound 8

TFA



AO-TEG-OH, 51

0.1M NaOAC, pH 4.6  
 glyoxyl peptide

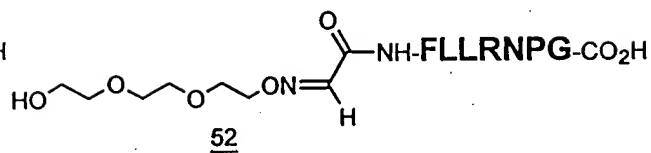


Figure 14

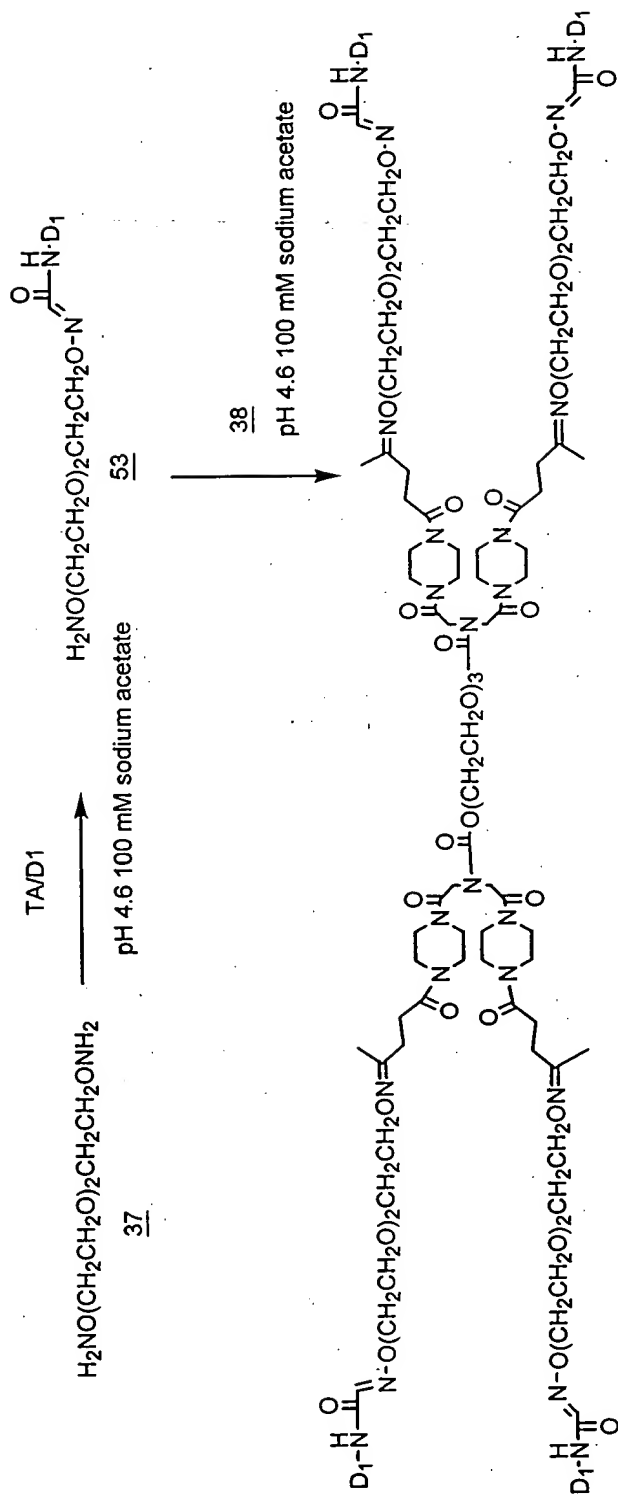


Figure 15





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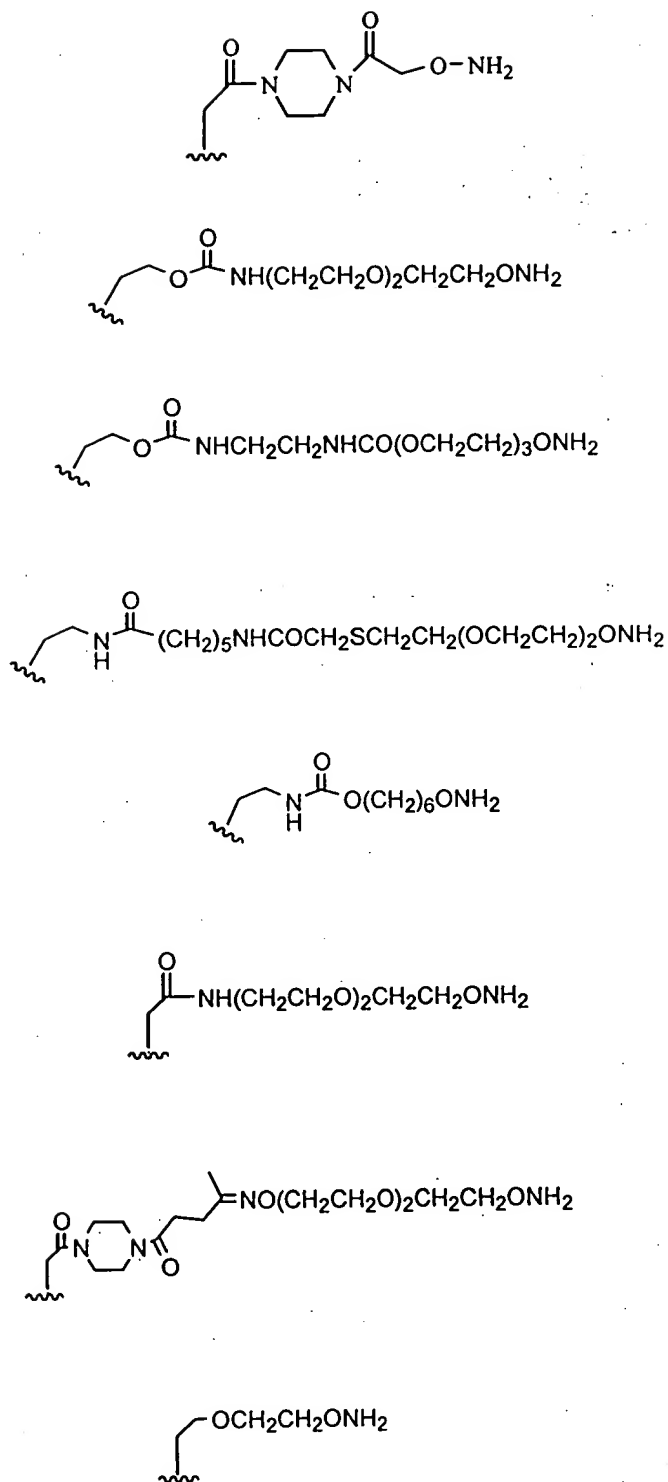
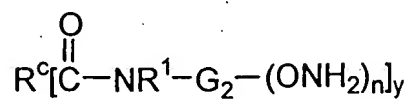


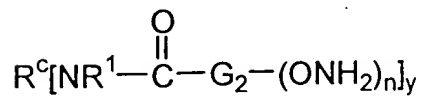
Figure 17

$$R^c[O-\overset{\overset{O}{\parallel}}{C}-NR^1-G_2-(ONH_2)_n]_y$$

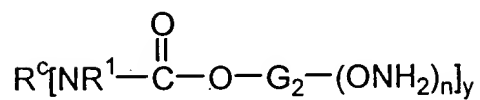
### Formula 3



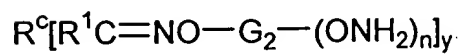
#### Formula 4



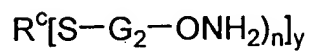
### Formula 5



### Formula 6



### Formula 7



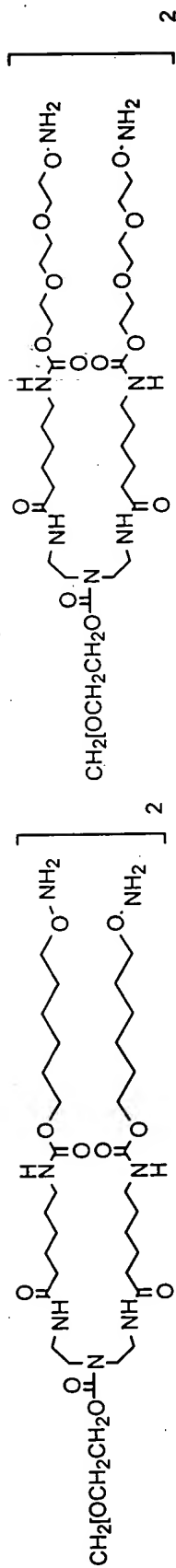
### Formula 8

Figure 18

$$\begin{array}{c} \text{H}_2\text{NO}-\text{G}_2 \\ | \\ \text{H}_2\text{NO}-\text{G}_2 \end{array} \text{N} \begin{array}{c} \text{O} \\ || \end{array} \text{R}_\text{C} \begin{array}{c} \text{O} \\ || \end{array} \text{N} \begin{array}{c} \text{G}_2-\text{ONH}_2 \\ | \\ \text{G}_2-\text{ONH}_2 \end{array}$$
$$\begin{array}{c} \text{H}_2\text{NO}-\text{G}_2 \\ | \\ \text{N} \\ | \\ \text{H}_2\text{NO}-\text{G}_2 \end{array} \text{---} \text{C}(=\text{O}) \text{---} \text{O} \text{---} \text{R}_\text{C} \text{---} \text{O} \text{---} \text{C}(=\text{O}) \text{---} \begin{array}{c} \text{G}_2\text{---}\text{ONH}_2 \\ | \\ \text{N} \\ | \\ \text{G}_2\text{---}\text{ONH}_2 \end{array}$$
$$\begin{array}{c} \text{H}_2\text{NO}-\text{G}_2 \\ | \\ \text{N} \\ | \\ \text{H}_2\text{NO}-\text{G}_2 \end{array} \text{C}(=\text{O}) \text{O}-(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_2\text{CH}_2\text{O}-\text{C}(=\text{O}) \begin{array}{c} \text{G}_2-\text{ONH}_2 \\ | \\ \text{N} \\ | \\ \text{G}_2-\text{ONH}_2 \end{array}$$
$$\begin{array}{c} \text{H}_2\text{NO}-\text{G}_2 \\ | \\ \text{N} \\ | \\ \text{H}_2\text{NO}-\text{G}_2 \end{array} \text{---} \text{C}(=\text{O}) \text{---} \text{O} \text{---} (\text{CH}_2)_n \text{---} \text{O} \text{---} \text{C}(=\text{O}) \begin{array}{c} \text{G}_2\text{---ONH}_2 \\ | \\ \text{N} \\ | \\ \text{G}_2\text{---ONH}_2 \end{array}$$
$$\begin{array}{c} \text{H}_2\text{NO}-\text{G}_2 \\ | \\ \text{N} \\ | \\ \text{H}_2\text{NO}-\text{G}_2 \end{array} \text{---} \text{C}(=\text{O}) \text{---} (\text{CH}_2)_n \text{---} \text{C}(=\text{O}) \text{---} \begin{array}{c} \text{G}_2\text{---ONH}_2 \\ | \\ \text{N} \\ | \\ \text{G}_2\text{---ONH}_2 \end{array}$$

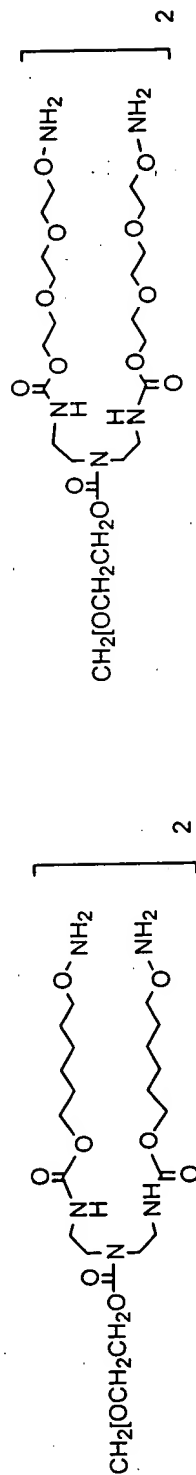
Formula 13

Figure 19



80

81



82

83

Figure 20

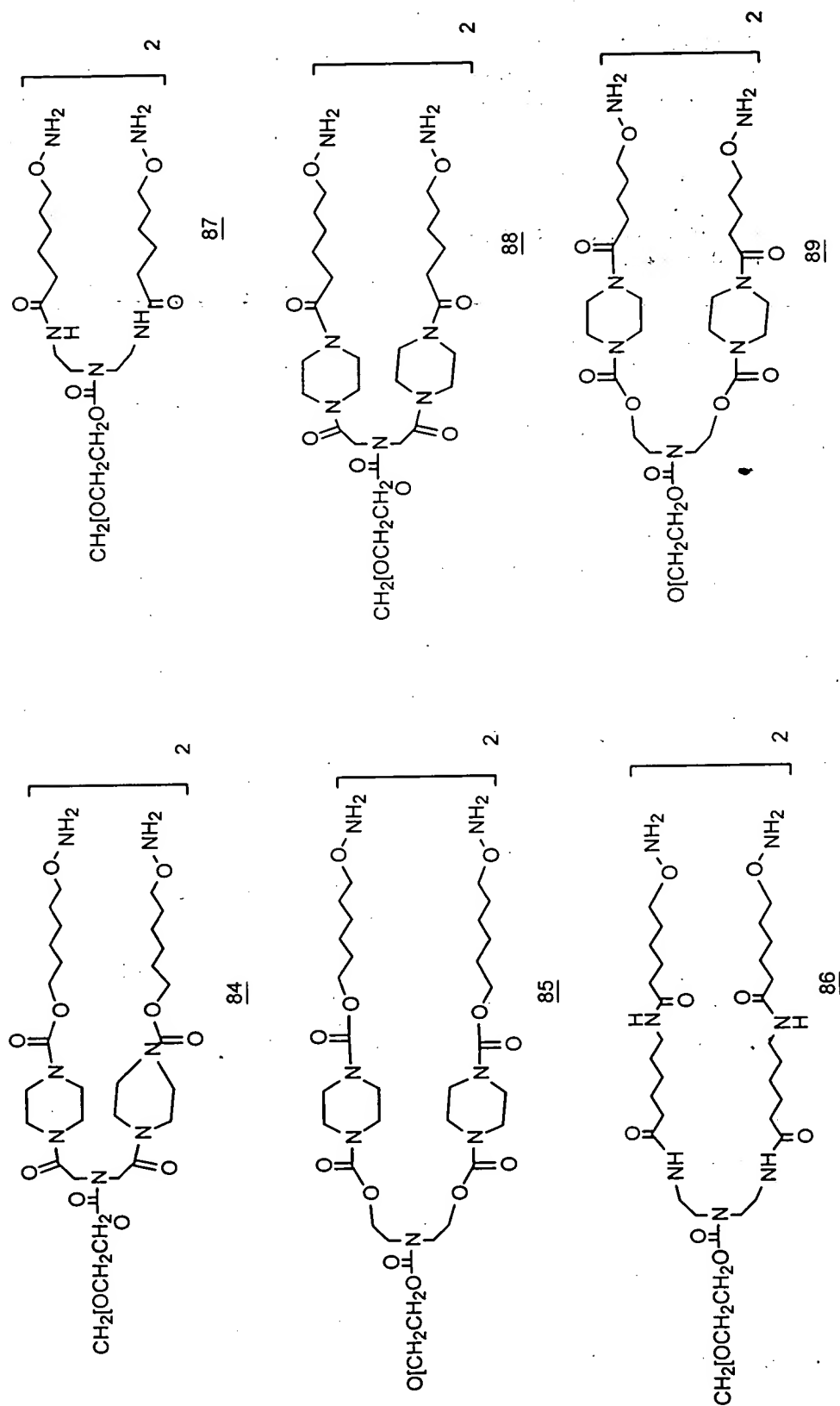


Figure 21

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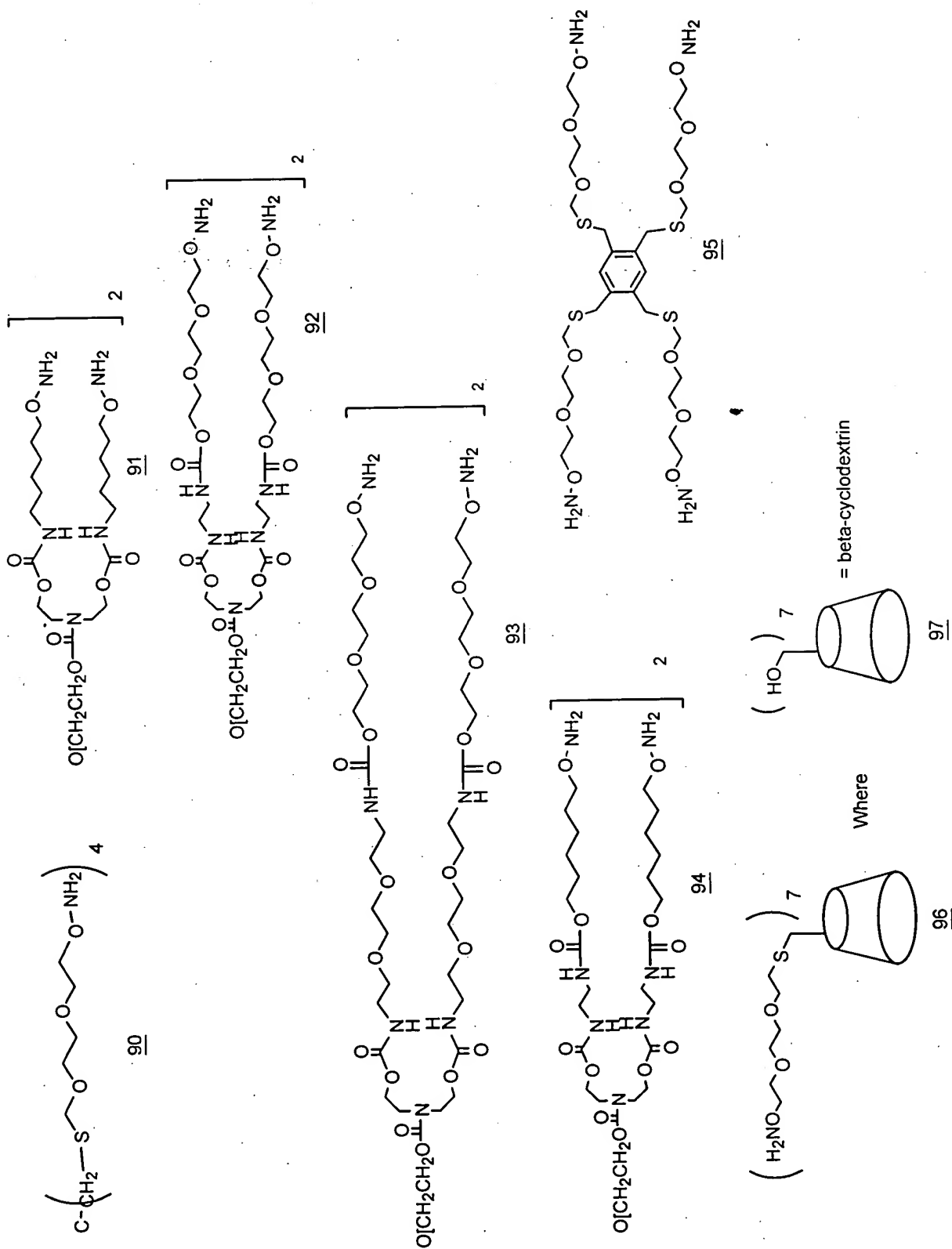


Figure 22

008090" 26506560

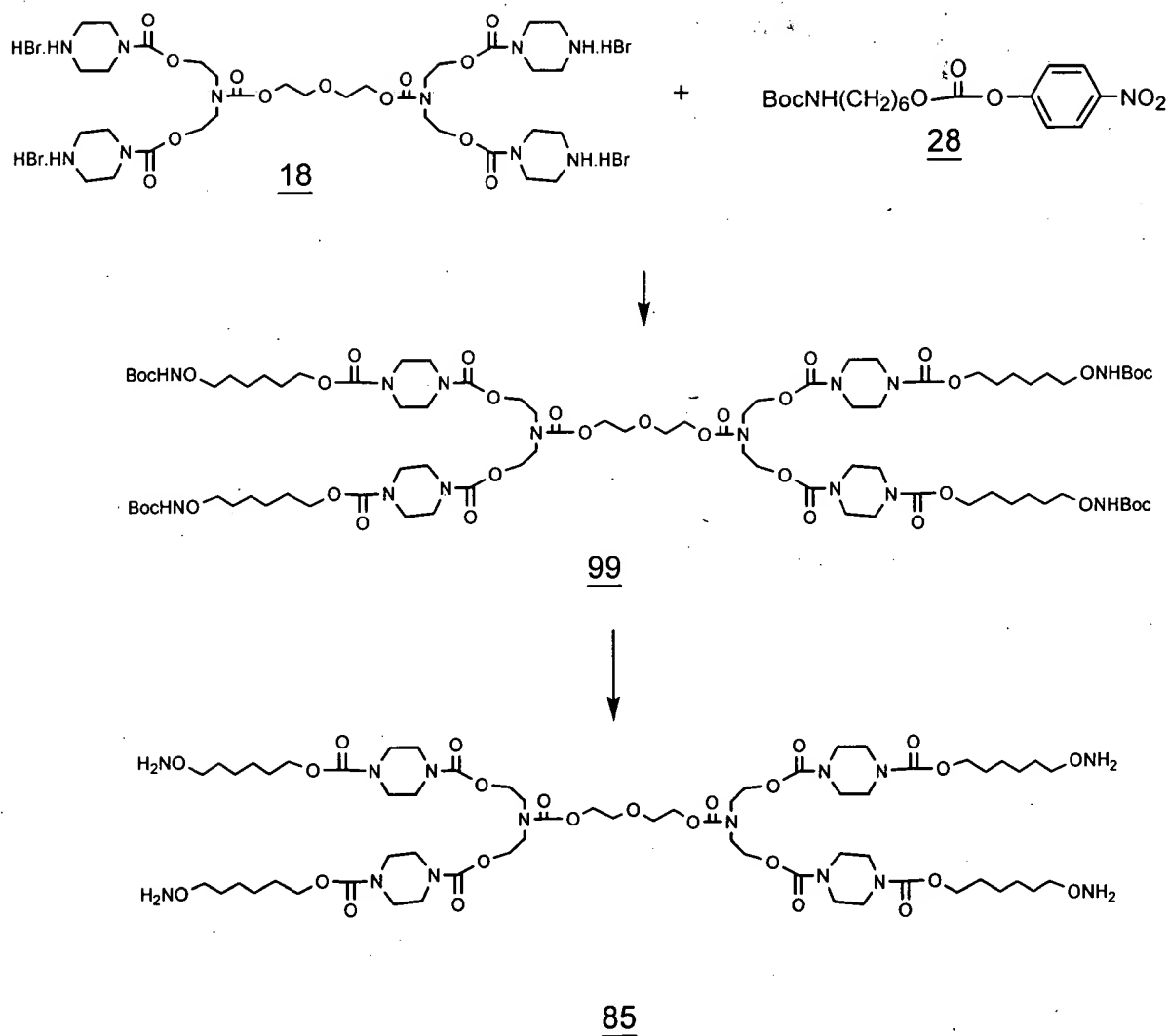


Figure 23

003090-26506560

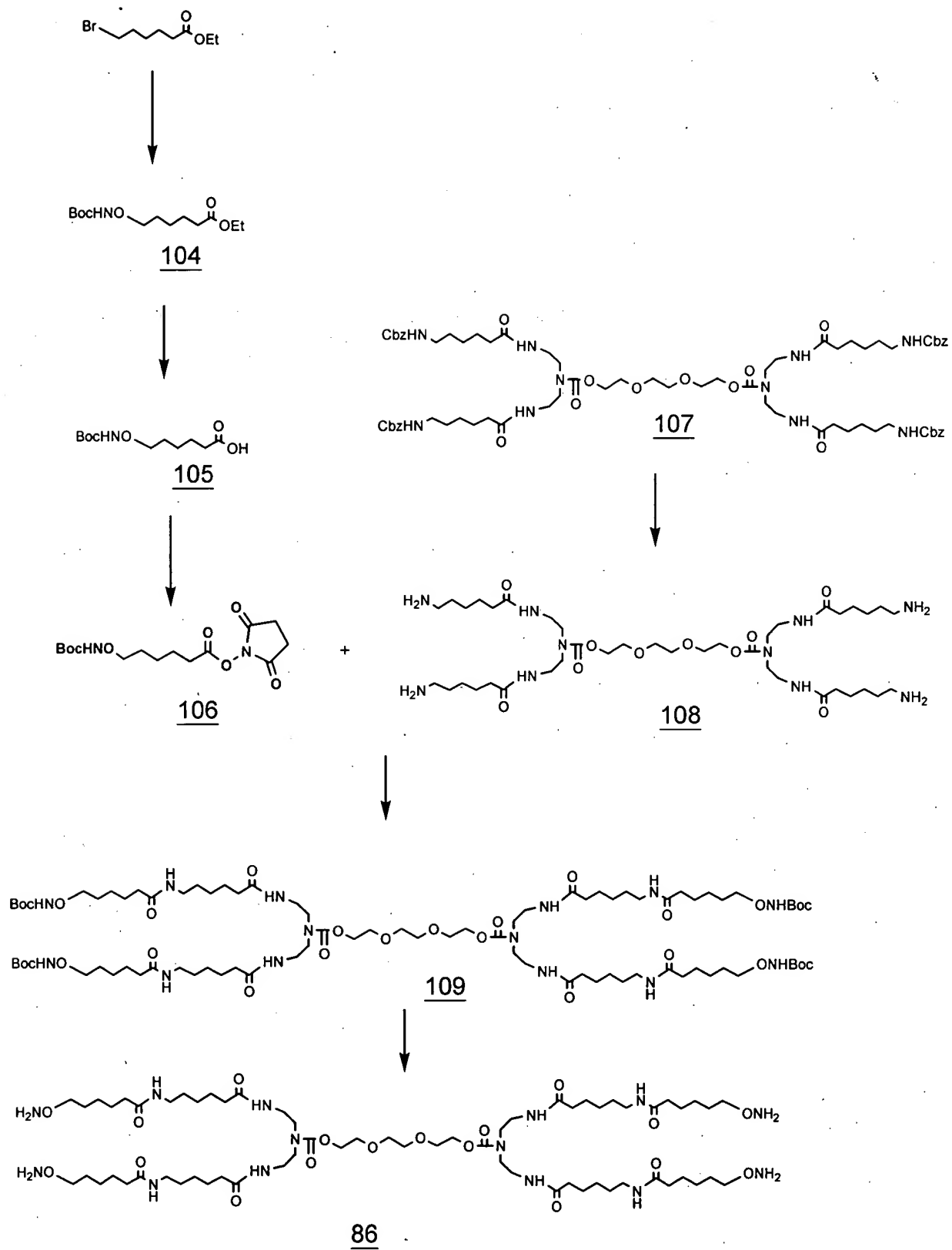


Figure 24



003090-26506560

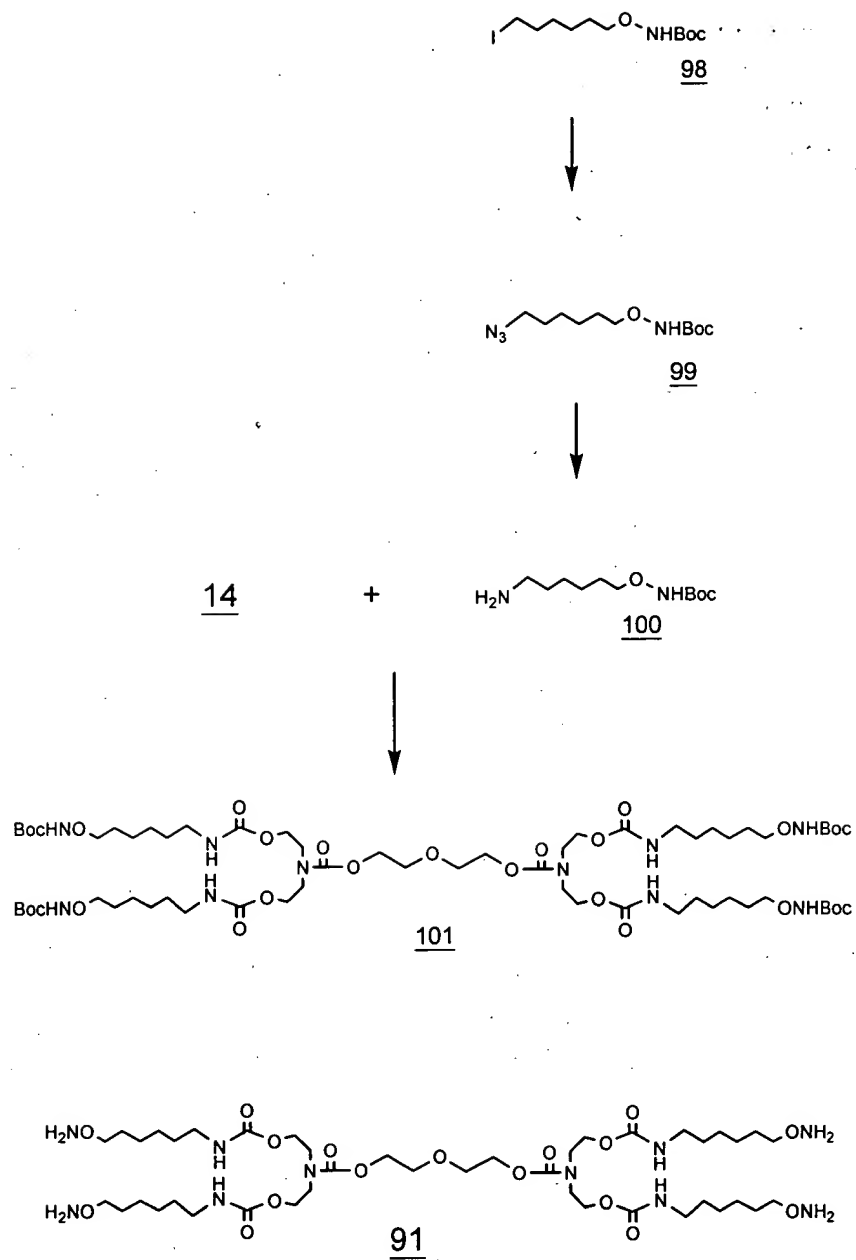


Figure 25

Figure 26

000090" 2650560

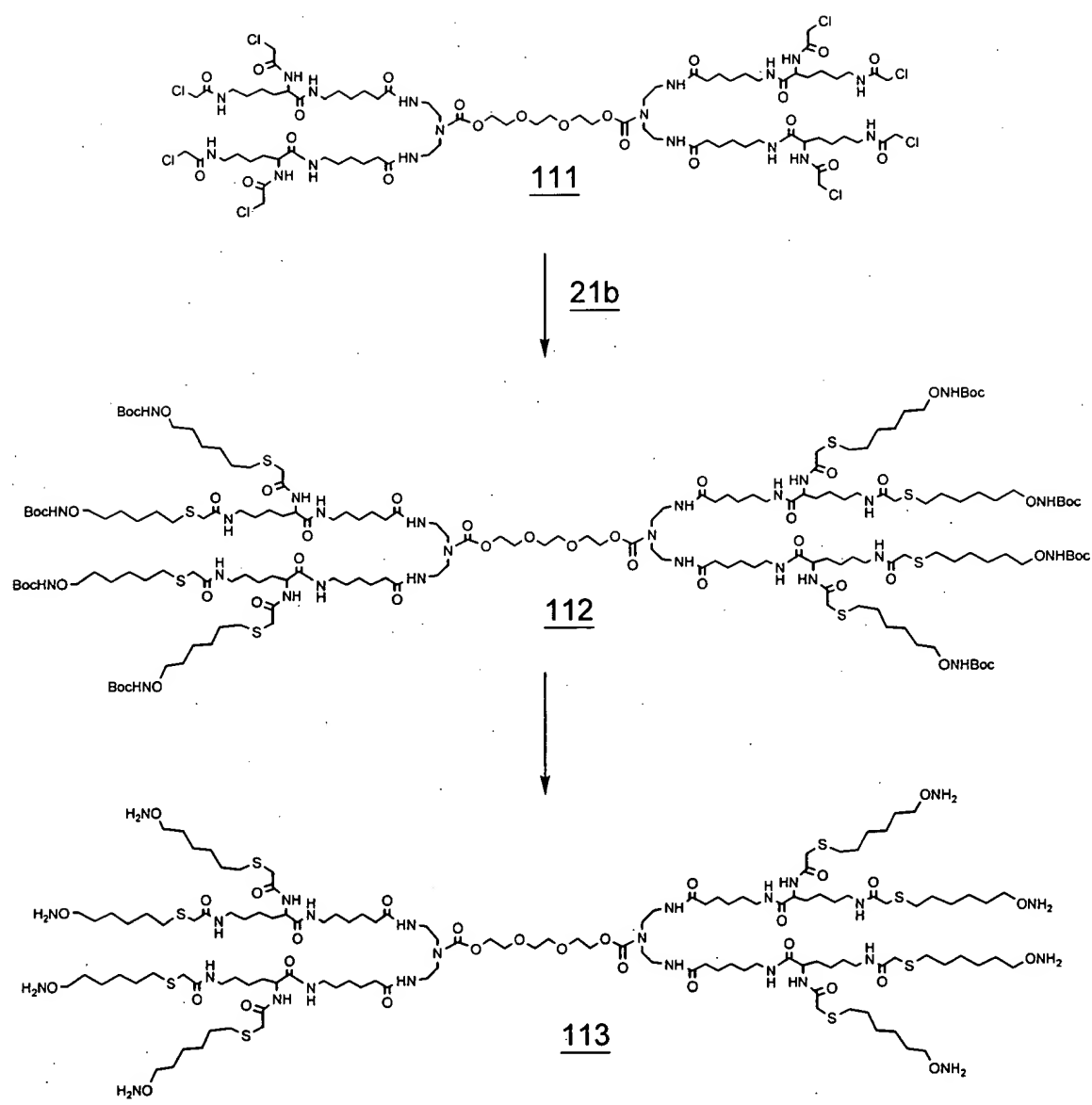


Figure 27

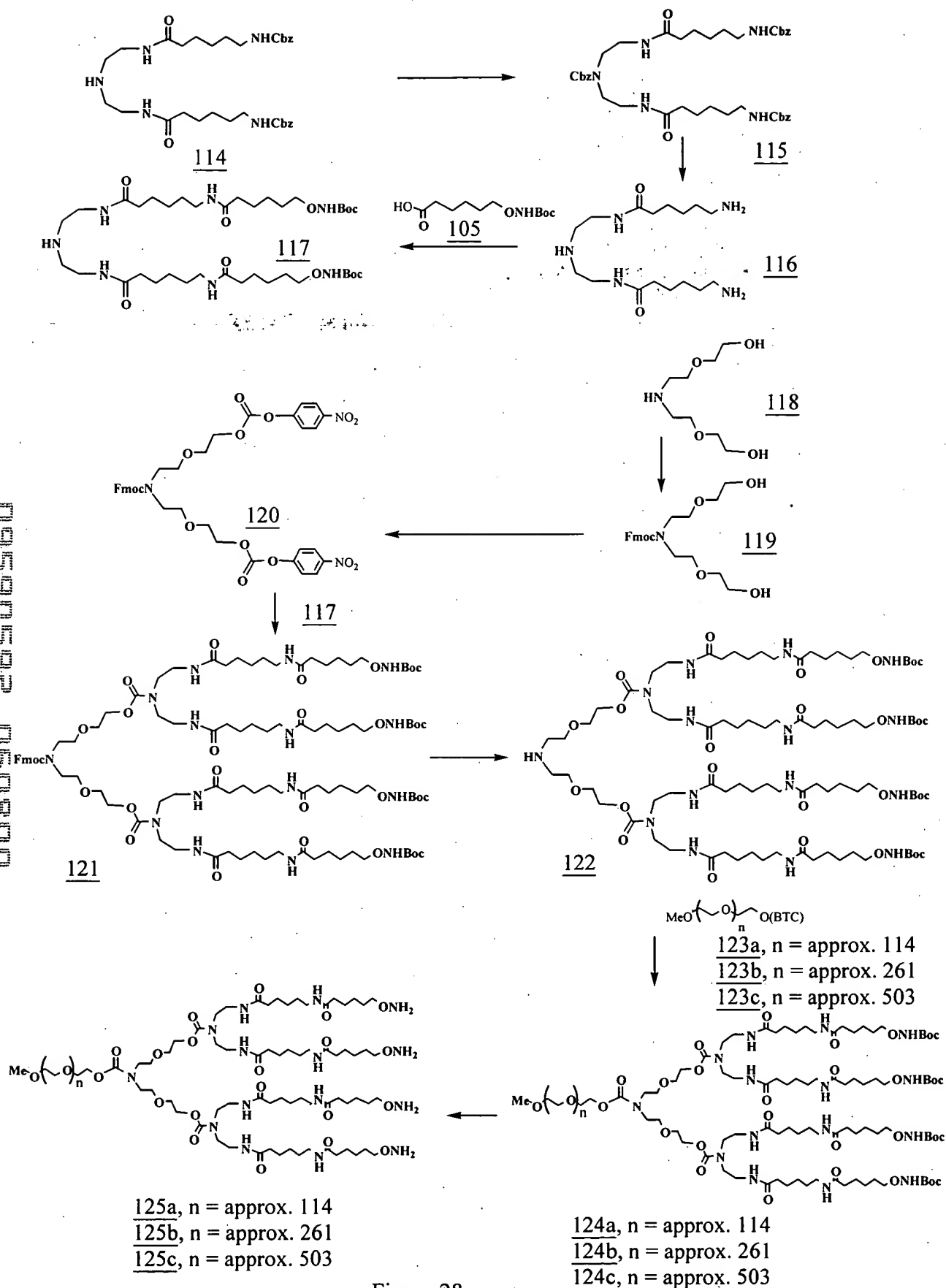
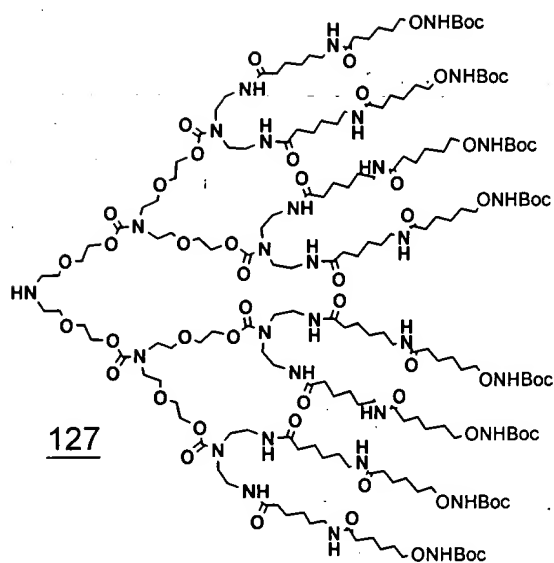


Figure 28

120

122



123c

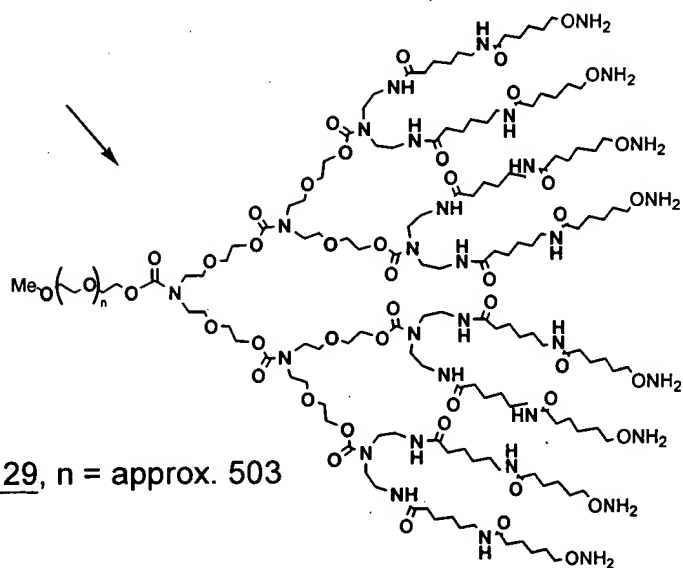
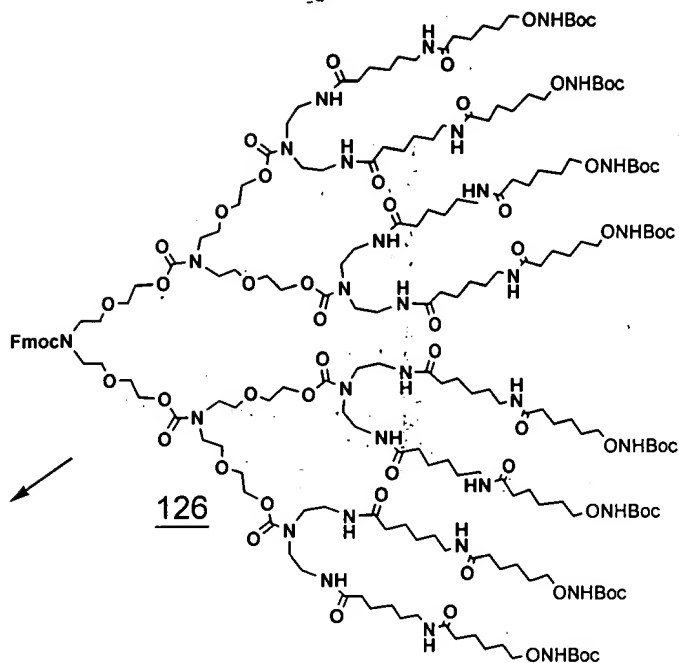
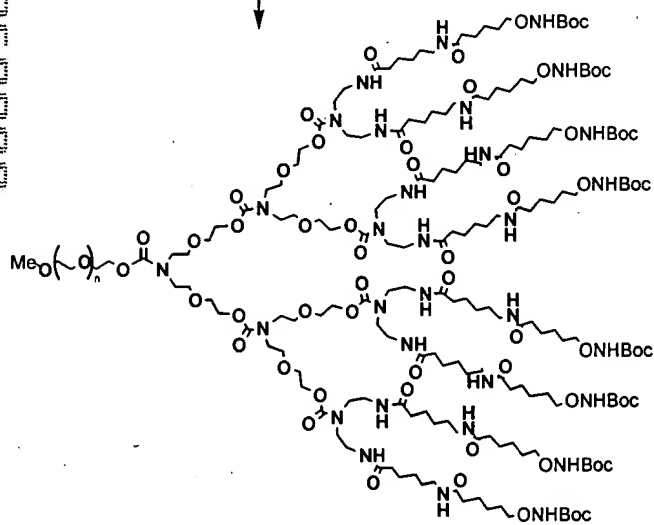


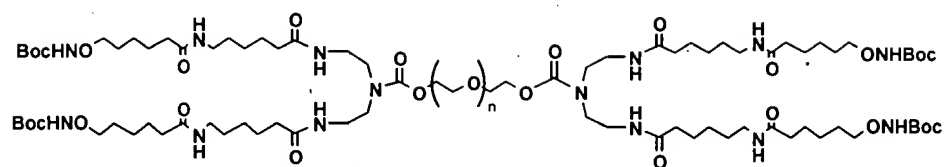
Figure 29

$$(\text{BTC})\text{O}\left(\text{---O---}\right)_n\text{O}(\text{BTC})$$

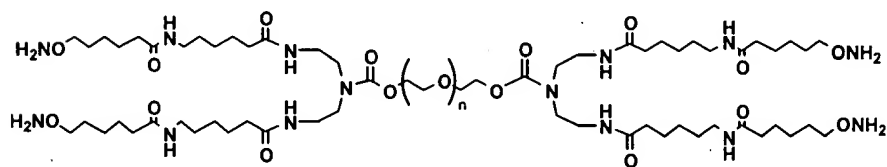
+

117

130, n = approx. 481



131, n = approx. 481



132, n = approx. 481

Figure 30

000000-26506560

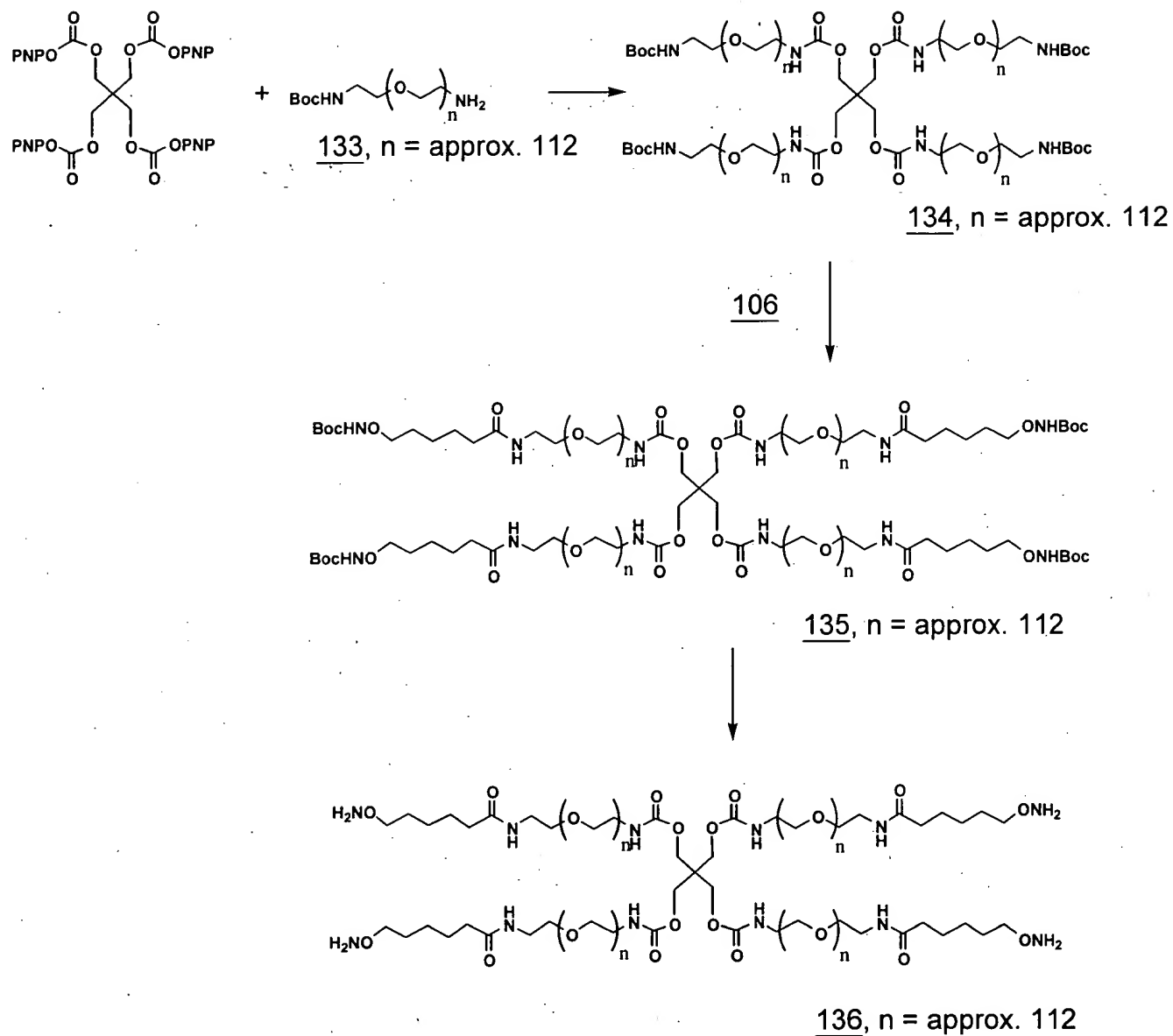


Figure 31

NC1=CC=C(C=C1C(=O)OCC)N + BrCCCCC(=O)Cl → BrCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**137**)

BrCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**138**)

BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N + HOCCCCC(=O)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**139**)

BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N + HOCCCCC(=O)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**140**)

BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N + HNCCCC(=O)OCCCC(=O)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**141**,  $n \approx 76$ )

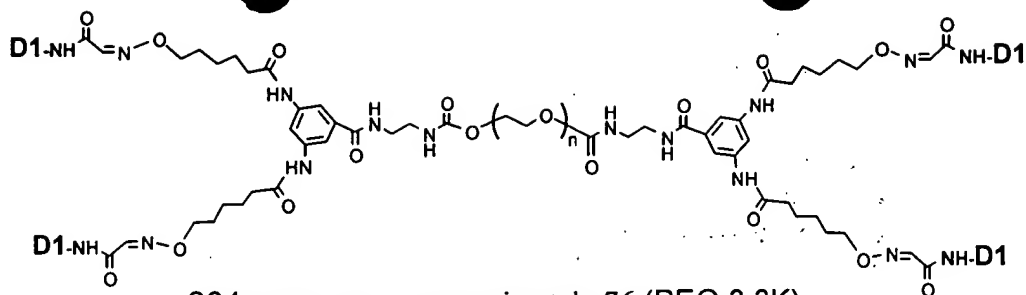
BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N + HNCCCC(=O)OCCCC(=O)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**142**,  $n \approx 76$ )

BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N + HNCCCC(=O)OCCCC(=O)N → BocNCCCCC(=O)NC1=CC=C(C=C1C(=O)OCC)N (**143**,  $n \approx 76$ )

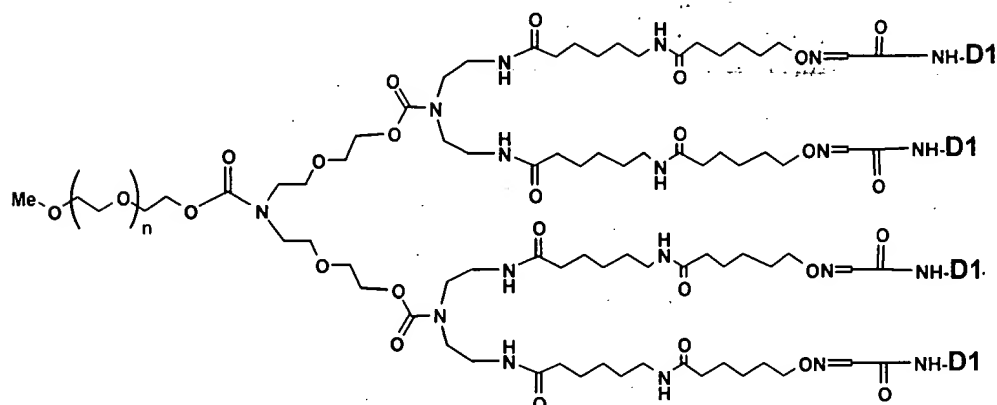
—



000000-26506560



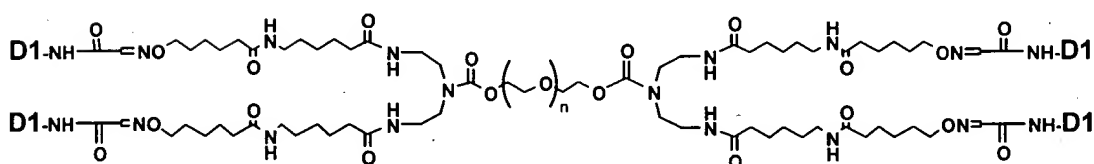
204; average  $n$  = approximately 76 (PEG 3.3K)



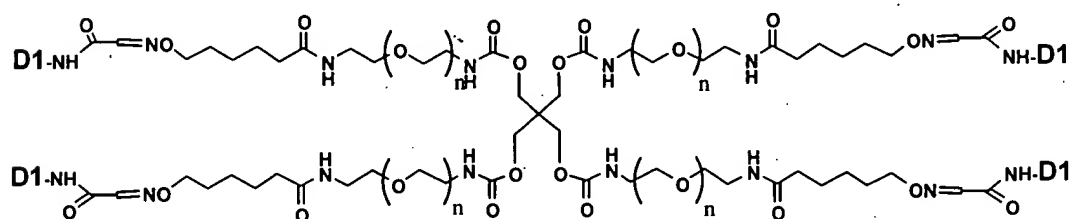
200; average  $n$  = approximately 503 (PEG 20K)

201; average  $n$  = approximately 114 (PEG 5K)

205; average  $n$  = approximately 261 (PEG 12K)

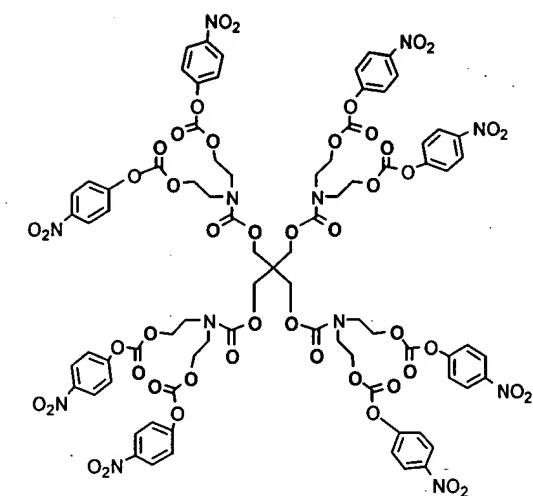


202; average  $n$  = approximately 503 (PEG 20K)

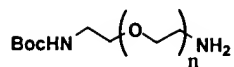


203; average  $n$  = approximately 125 (PEG 5K)  
total PEG = 20K

Figure 33



Compound 50a



133,  $n = \text{approx. } 112$

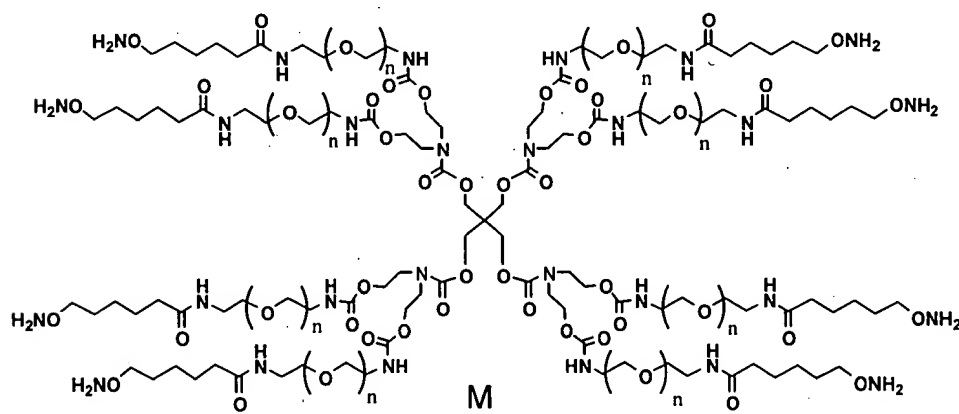
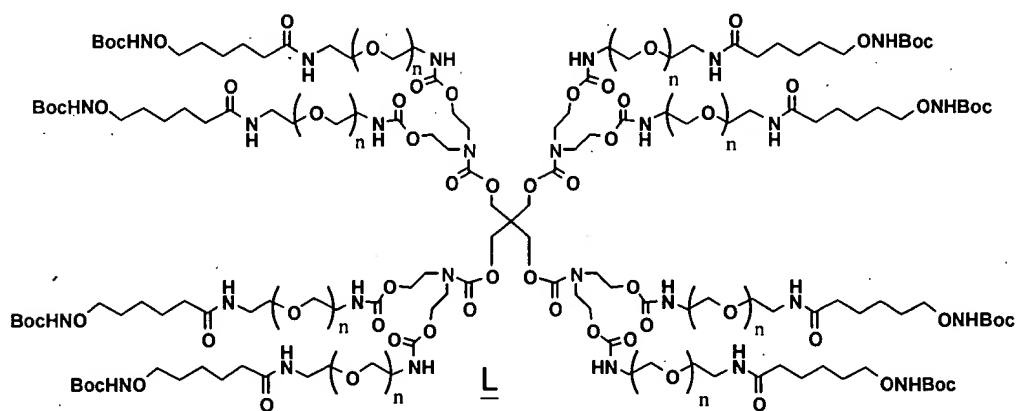
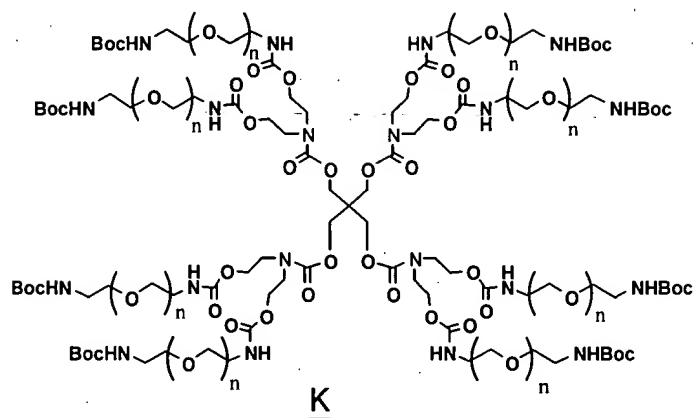


Figure 34

008090" 26506560

008090" 26506560

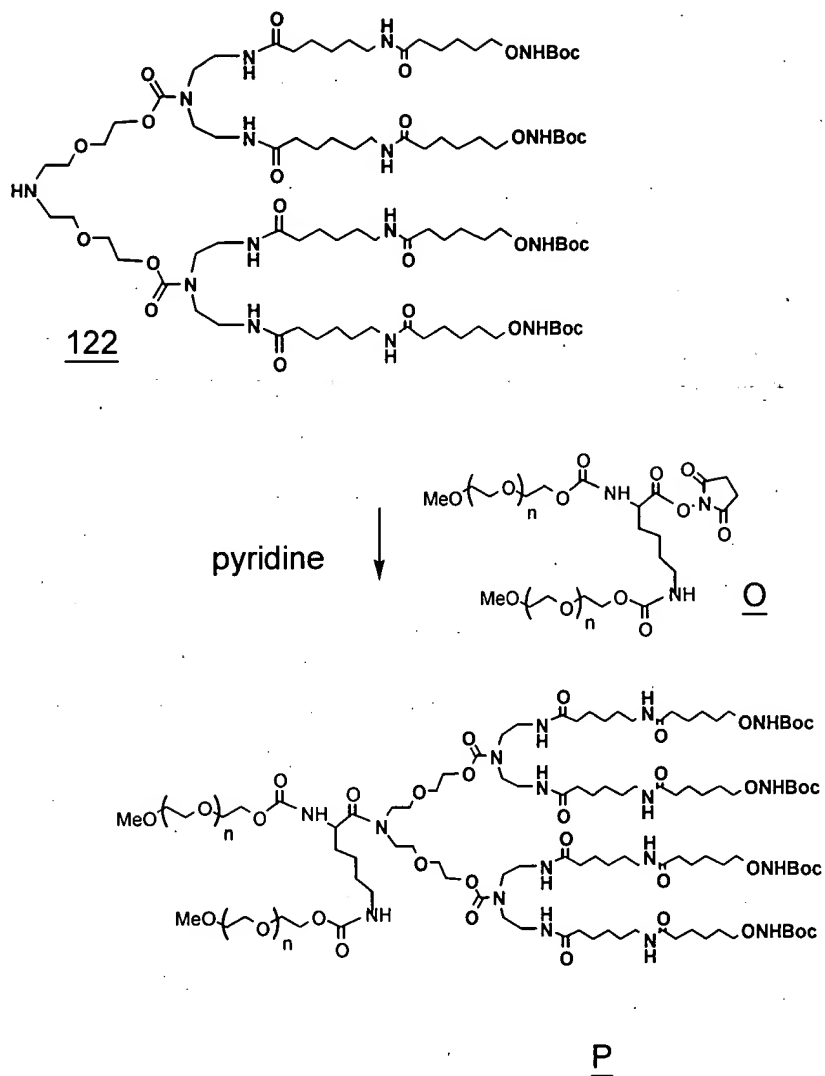


Figure 35